

REMARKS/ARGUMENTS

Claims 1-6 and 8-22 are active in this application.

In the Official Action, it appears that the Examiner has both withdrawn and maintained the rejection under 35 USC §102(b) in view of WO'693. However, as apparent from the statement made on page 4 of the Official Action ("Response to Arguments), the rejection was withdrawn with respect to the method claims but maintained the rejection in view of the kit claim, Claim 7. Claim 7 has been cancelled and therefore this rejection is no longer applicable.

The Examiner has now raised a new rejection alleging that the claims would have been obvious in view of WO'693 and of US Patent No. 6,342,387 (US'387).

As explained previously and recognized in the rejection, WO '693 describes that essential steps of the method are to bind the cells with the solid carrier then lyse the cells in a manner that permits the nucleic acids to also bind to this solid carrier (see page 4, 1<sup>st</sup> paragraph and 3<sup>rd</sup> paragraph). This method is different from the claimed method where the cells in the sample are directly lysed after which the nucleic acids are bound to the solid-phase carrier. (see page 6 of the Official Action: "Dzieglewska et al. do not explicitly disclose that the lysis solution be applied to the sample comprising nucleated cells prior to contacting the lysed, nucleated cells to a solid phase."

For this aspect of the claimed method, US'387 is cited.

According to the rejection, U.S. '387 describe lysing a biological sample (e.g. blood – column 3, lines 10-20) followed by binding with a DNA binding carrier (see for example, column 2). In view of this, the Examiner has taken the position that it would have been obvious to first lyse the cells prior to binding with the carrier having a particle size in ranges claimed.

However, the rejection is based on a fundamental misunderstanding of what is described in the '387 patent. That is, U.S. '387 does not describe lysis followed by contacting with a solid phase DNA carrier but rather that lysis and binding occur at the same time. The rejection outlined in the Official Action refers to the summary of the invention where it describes a lysing solution put into contact with a DNA binding carrier. What this actually means is that lysis and DNA binding occur simultaneously. In fact, the intent of this wording in the Summary portion of the '387 patent is made quite clear by the Examples. In Example 1 (col. 7), a lysing solution A including a number of components such as Urea, NaCl etc also comprising a DNA carrier (see col. 7, lines 49-50) is mixed with whole blood (see col. 7, lines 33-34).

Moreover, this simultaneous lysing and binding is evident from the Background section of U.S. '387 where they emphasize the advantage of their invention as not requiring manipulation steps (e.g., centrifugation) between the lysing and binding because they are accomplished at the same time. Thus, like WO '693, U.S. '387 teaches away from the claimed invention requiring lysis first and binding second.

As a further basis for patentability, it was previously explained why the claimed invention has numerous advantages for real-world applications. As shown by a comparison of the Examples according to the present invention and Comparative Example 1, the amount of nucleic acids recovered is superior in the present invention (see Table 1 reproduced below from the specification at page 33). Comparative Example 1 uses the phenol-chloroform extraction method which takes much longer (about 3 hours) compared to the present invention.

By using the method for extracting nucleic acids of the invention and the reagent thereof, nucleic acids can be purified from blood etc. in a large amount and a high purity, conveniently within a short period at a low cost. Also, the invention establishes a method

that uses no toxic or corrosive solvent and thus is not harmful to working environment and workers. Therefore, the method is widely applicable to the fields of gene engineering, genetic diagnosis, genetic therapy, genome chemistry, genomic drug development, and the like. Moreover, the method is capable of automation of the treatment.

Such superior results are not disclosed or suggested by the art cited in the Official Action.

As even further basis for the patentability of the claims, Applicant emphasizes the importance of the average particle size of 0.01 to 1000  $\mu\text{m}$  as recited in Claim 1. To this end, Applicant submits an executed Rule 132 Declaration in support of this limitation as well. The experiments discussed in the specification and in the declaration show the importance of using an insoluble solid-phase carrier having an average particle size of 0.01 to 1000  $\mu\text{m}$  in a method as claimed in the above-identified application. Portions of the Declaration are reproduced below for convenience.

In accordance with the same method as in Example 1 of the present application but using polystyrene particles having an average particle size of 5 nm instead of particles having an average particle size of 20  $\mu\text{m}$  and having polystyrene surface and an iron oxide inner part, DNA was extracted and eluted from the solid carrier. Then, DNA and the solid carrier were separated by centrifugation at 15,000 r.p.m. for 1 hour. Measurement of absorbance showed an absorbance of about 0.2 at 320 nm, which revealed that there were minute particles which could not be separated. Continuous centrifugation for 1 hour under the same conditions decreased the absorbance at 320 nm to 0.17 but the absorbance did not become 0. Absorbance was measured from 320 nm to 240 nm under the resulting conditions. Due to the contamination of minute particles, the peak at around 260 nm, which is attributed to DNA, was not clear and the quantitative determination and purity determination of DNA was impossible. Accordingly, use of smaller size particles having an average particle size of less than 0.01  $\mu\text{m}$  made it difficult to separate particles and DNA, so that DNA having a high purity was not obtained.

In accordance with the same method as in Example 1 of the present application but using polystyrene particles having an

average particle size of 5 mm instead of particles having an average particle size of 20  $\mu$ m, DNA was extracted and eluted from the solid carrier. As shown in the table below, the amount of DNA recovered was remarkably decreased.

WO 98/51693 and U.S. '387 in view of Ekeze et al and/r Belley et al alone or in combination.

Notably, Ekeze is cited simply to teach the isolation of nucleic acids from blood samples but when combined with WO '693 and U.S. '387 fail to describe or suggest the invention claimed where the cells in the sample are directly lysed after which the nucleic acids are bound to the solid-phase carrier. Moreover, there is nothing in either publication which would suggest modifying the WO '693 and U.S. '387 disclosure to do what is claimed because both WO '693 and U.S. '387 teach away from doing what is claimed.

In addition, Belley is cited simply to discuss nucleic acid separation from tissue but when combined with WO '693 and U.S. '387 fail to describe or suggest the invention claimed where the cells in the sample are directly lysed after which the nucleic acids are bound to the solid-phase carrier. Moreover, there is nothing in either publication which would suggest modifying the WO '693 and U.S. '387 disclosures to do what is claimed because WO '693 and U.S. '387 teach away from doing what is claimed.

The rejection of the claims over WO 96/18731, U.S. '387, Belley et al, and/or Ekeze et al are believed to be unsustainable as the present invention is neither anticipated nor obvious.

Withdrawal of these rejections is respectfully requested.

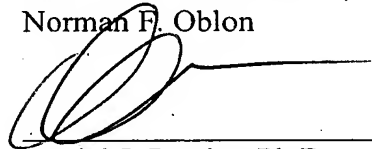
Application No. 10/627,780  
Reply to Office Action of November 9, 2006

A Notice of Allowance for all pending claims is earnestly solicited.

Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, he is encouraged to contact Applicants' undersigned representative.

Respectfully submitted,

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A handwritten signature in black ink, appearing to read 'Daniel J. Pereira', is written over a horizontal line.

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